SUPPORT FOR THE AMENDMENTS

Newly-added Claims 48-59 are supported by the specification. Accordingly, no new matter is believed to have been added to the present application by the amendments submitted above.

REMARKS

Claims 30-34 and 48-59 are pending. Favorable reconsideration is respectfully requested.

In the amendments submitted above Claims 30-34 are unchanged. Claims 48-59 have been added to replace Claims 35-47 and address the concerns set forth in the Office Action. The subject matter of Claim 38 has been canceled from the claims.

Claim 48 is limited to a hairpin oligoribonucleotide (hairpin RNA or shRNA) comprising the sense and antisense strands of the oligonucleotide (siRNA) as claimed in Claim 30, as defined in c) of claim 35. Since Claim 48 is directed to an RNA molecule, the oligonucleotide of Claim 30 is an oligoribonucleotide (RNA), e.g., it has two ribonucleotides at the 3' ends of its sense and antisense strands, as specified in Claim 30 and in Claim 48.

Claims 51 and 52 are directed to an expression cassette and an expression vector for a siRNA or a shRNA, comprising an isolated DNA sequence consisting of a DNA sequence encoding the oligonucleotide as claimed in Claim 30, or the derived shRNA as defined above. Support for this amendment is found in the specification page 12, line 15 to page 15, line 6 and in particular in page 14, lines 15-21,34-39 and in page 15, lines 4-6.

As set forth in Claim 30, the present invention relates to a double-stranded oligonucleotide comprising two strands of 19 to 23 nucleotides, each strand consisting, from 5' to 3', of a sequence of 17 to 21 ribonucleotides and two deoxyribo- or ribonucleotides, the 17 to 21 ribonucleotide RNA sequences of said strands being complementary and the two nucleotides of the 3' ends being protruding,

where the RNA sequence of the sense strand or positive strand is selected from the group consisting of a 17 to 21 ribonucleotide fragment of a transcript of a protein kinase CK2 beta-subunit which is included between positions 80-100, from the ATG codon, with

reference to the human transcript sequence SEQ ID NO: 90, and a 17 to 21 ribonucleotide fragment having at least 80 % identity with the preceding fragment,

where the sequence of the sense strand or positive strand is selected from the group consisting of the sequences SEQ ID NO: 67, 83 and 86, and

where the double-stranded oligonucleotide inhibits specifically more than 80% of the expression of the protein kinase CK2 beta-subunit and of the corresponding mRNA in human cell culture at a concentration of between 1 and 200 nM.

The rejections of claims 35-38 and 40-44 under 35 USC §102 (b) as being anticipated by Mukerji et al. (US 6,287,866) and Frudakis et al., (US 6,225,054) are believed to be obviated by amendment and traversed in part.

The siRNA of the invention is a 19 to 23 bp siRNA targeting positions 80-100 of the human CK2 beta-subunit transcript starting from the ATG codon (claims 30-34).

Neither of the cited references disclose:

- a shRNA comprising both strands of the claimed siRNA connected by a short loop,
- a siRNA/shRNA expression cassette/vector comprising an isolated DNA sequence consisting of a DNA sequence encoding: (i) one or both strands of the siRNA of claim 30 or (ii) the shRNA as defined above, and
- a pharmaceutical composition comprising said siRNA, shRNA or vector.

Mukerji el al. disclose a protein expression plasmid which has improved genetic stability (column I, line 58 to column 2, line 5), said plasmid comprising : (i) a nucleotide sequence encoding a protein operably linked to a promoter, (ii) a nucleotide sequence encoding the human CK2 alpha-subunit, (iii) a nucleotide sequence encoding the full-length human CK2 beta-subunit, (iv) a nucleotide sequence encoding a peptidase, and (v) a nucleotide sequence encoding a bacterial resistance marker (column 2, lines 10 to 28 and figure 1B).

Frudakis el al. disclose a DNA vaccine comprising a 335 bp DNA fragment (SEQ ID NO: 217) of the human CK2 beta-subunit encoding an epitope of an antigenic/immunogenic polypeptide (column 2, lines 16 to 45; column 3, line 60 to column 4, line 6; column 14, lines 37 to 55).

In view of the foregoing, Mukerji et al. and Frudakis et al. fail to disclose the claimed double-stranded oligonucleotide. Accordingly, the subject matter of the pending claims is not anticipated by that reference. Withdrawal of these grounds of rejection is respectfully requested.

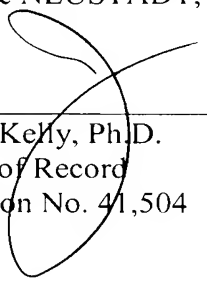
The objection to the claims and rejections of the claims under 35 U.S.C. §112, first and second paragraphs, are believed to be obviated by the amendment submitted above. Accordingly, withdrawal of these grounds of rejection is respectfully requested.

Regarding the Restriction Requirement, Applicants note that newly-added Claim 59 corresponds to previously-pending Claim 47. Claim 59 depends indirectly from Claim 30. Since Claim 30 is allowable as discussed above, Claim 59 is allowable by virtue of its dependence from Claim 30. Accordingly, rejoined to Claim 59 is requested.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



James J. Kelly, Ph.D.
Attorney of Record
Registration No. 41,504

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 08/03)